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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/651,668	08/28/2003	Alexei Brooun	SYR-ISPA-5001-C1	9129
32793	7590	02/13/2008		
TAKEDA SAN DIEGO, INC. 10410 SCIENCE CENTER DRIVE SAN DIEGO, CA 92121			EXAMINER KIM, ALEXANDER D	
			ART UNIT	PAPER NUMBER
			1656	
			MAIL DATE	DELIVERY MODE
			02/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/651,668

Applicant(s)

BROOUN ET AL.

Examiner

Alexander D. Kim

Art Unit

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 4, 6, 9, 18, 19 and 21-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 19 and 24 is/are allowed.
- 6) ☒ Claim(s) 1, 4, 6, 9, 18 and 21-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Application Status

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/06/2007 has been entered.

In response to the previous Office action, a Final rejection (mailed on 10/24/2007), Applicants filed a response and amendment received on 11/05/2007. Said amendment cancelled Claims 2-3, 5, 7-8, 10-17 and 20; amended Claims 1, 6 and 23.

Claims 1, 4, 6, 9, 18-19 and 21-24 are pending in the instant Office action and will be examined herein.

Withdrawn-Objections to the Specification

2. The previous objection of specification because it is unclear which protein is used in the actual crystallization in the Example 2 is withdrawn by virtue of Applicants' argument.

Maintained-Claim Rejections - 35 USC § 112

3. Claims 1, 4, 6, 9, 18 and 21-23 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous Claims 1, 4, 6, 9-10, 18 and 20-23. In response to this rejection, applicants have cancelled Claims 2-3, 5, 7-8, 10-17 and 20; amended Claims 1, 6 and 23 and traverse the rejection as it applies to the newly amended claims. Applicants' argument has been fully considered but is not deemed persuasive for the following reasons.

Applicants traverse the instant rejection on the basis that the written description requirement is satisfied when "the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed" and "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter" (see bottom of page 4 to top of page 5). Applicants argue the claimed subject matter does not need to be described literally in order to satisfy the description requirement.

The Examiner acknowledges and agrees with the applicants argument above as long as the claimed subject matter is in possession by one skilled in the art in view of the instant disclosure, or the instant disclosure teach a sufficient structure and functional

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correlation for the full scope of claimed subject matters which may not have literal description.

As noted in the previous office action, the breadth of claim 1 is drawn to a very widely varying composition comprising any crystal (including co-crystal if bound ligand is in the protein), wherein the crystal is consist of 1-314 of SEQ ID NO: 1 and the crystal has a crystal lattice in a $P4_122$ and the unit cell dimensions $a=88.80 \text{ \AA}$, $b=88.80 \text{ \AA}$, $c=174.99 \text{ \AA}$ and $\alpha=\beta=\gamma=90^\circ$, wherein the composition includes any molecule (e.g., ligand(s)) or combination of molecules. It is also note that the instant amended limitation reciting "wherein said protein forms a complex with a ligand" (wherein a ligand is a genus of any molecule) in Claims 1 and 6 can be interpreted as binding capability of said protein as well as the co-crystal (or a method of making a co-crystal). Thus, one skilled in the art would not be able to possess the full scope of claimed invention by the virtue of instant disclosure lacking the disclosure of correlation between structure of composition and function of forming a protein crystal. The breadth of claim 6 is drawn to a very widely varying method for forming a crystal of a protein (optionally), which is consist of 1-314 of SEQ ID NO: 1, in any suitable conditions encompassing unlimited mother liquor composition and their concentration as well as having unlimited molecule(s), compound(s) or any combination thereof. Thus, one skilled in the art would not be able to possess the full scope of claimed method by the virtue of instant disclosure lacking the disclosure of correlation between structure (i.e., a precipitant and a protein solution) and function (i.e., conditions suitable for forming a protein crystal when the suitable condition results in a protein crystal). The fact that there are many

publication or disclosure of protein crystallization in general has very minimal (almost none) support for providing the representative species for the instant claims because every crystallization is case by case basis, specially those publication or disclosure is not about the crystallization of a protein consisting of residues 1-314 of SEQ ID NO: 1. For the reasons above and the previous written description rejection, the instant rejection is maintained.

4. Claims 1, 4, 6, 9, 18 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for a crystal or a method for preparing a co-crystal of a polypeptide consisting of residues 1-314 SEQ ID NO: 1 by a method of crystallizing a ternary complex consisting of said polypeptide with ligands (IPP+Risedronate, see specification page 49), that results in a crystal having the space group P4₁22 and the unit cell dimensions $a=88.80 \text{ \AA}$, $b=88.80 \text{ \AA}$, $c=174.99 \text{ \AA}$ and $\alpha=\beta=\gamma=90^\circ$, does not reasonably provide enablement for all crystals and methods comprising the steps of using any suitable condition for the preparation of the co-crystal as broadly encompassed by the breadth claims in the presence of any molecule as a ligand.

The rejection was stated in the previous office action as it applied to previous Claims 1, 4, 6, 9-10, 18 and 20-23. In response to this rejection, applicants have cancelled Claims 2-3, 5, 7-8, 10-17 and 20; amended Claims 1, 6 and 23 and traverse the rejection as it applies to the newly amended claims. Applicants' argument has been fully considered but is not deemed persuasive for the following reasons.

Applicants traverse the instant rejection because the standard for determining whether the specification meets the enablement requirement is by a determination whether any undue experimentation is necessary.

As noted in the previous office action, the undue experimentation is necessary for one skilled in the art to make and use the full scope of claimed subject matter for the following reasons. The breadth of claim 1 is drawn to a very widely varying composition comprising any crystal (including co-crystal if bound ligand is in the protein), wherein the crystal is consist of 1-314 of SEQ ID NO: 1 and the crystal has a crystal lattice in a P4₁22 and the unit cell dimensions $a=88.80 \text{ \AA}$, $b=88.80 \text{ \AA}$, $c=174.99 \text{ \AA}$ and $\alpha=\beta=\gamma=90^\circ$, wherein the composition includes any molecule (e.g., ligand(s)) or combination of molecules. The breadth of claim 6 is drawn to a very widely varying method for forming a crystal of a protein (optionally), which is consist of 1-314 of SEQ ID NO: 1, in any suitable conditions encompassing unlimited mother liquor composition and their concentration as well as having unlimited molecule(s), compound(s) or any combination thereof. It is also note that the instant amended limitation reciting "wherein said protein forms a complex with a ligand" (wherein a ligand is a genus of any molecule) in Claims 1 and 6 can be interpreted as binding capability of said protein as well as the co-crystal (or a method of making a co-crystal). Examiner acknowledges that a routine experiment does not automatically require an undue experimentation. It is true that one skilled in the art can screen very widely varying crystallization condition using commercially available kit and robotic operation without undue experimentation. However, to make and use such screening method to be a "conditions suitable for

formation of a protein crystal" which encompasses a forming a crystal of a protein consist of residues 1-314 of SEQ ID NO: 1, and optionally with any ligand which binds to the protein to form co-crystal, would require a undue experimentation in view of very broad claimed crystal and/or claimed method of crystallization and unpredictability of forming a genus of claimed protein crystal. The modernization of procedure does make the process of screening faster but does not decrease the unpredictability nature of protein crystallization. This very unpredictable nature of protein crystallization is the reason one skilled in the art first attempt to screen as broad crystallization conditions as possible, which is also supported by Applicants' own disclosure reciting the wide range of crystallization conditions disclosed by the present invention provide guidance to further explore for new conditions to grow the claimed crystal" (see bottom of page 8, Remark filed on 08/06/2007). The said further exploration is what makes one skilled in the art to require an undue experimentation for protein crystallization, especially when the claims are drawn to a very widely varying genus as described above in the breadth of claims. Thus, the instant disclosure and the prior art failed to provide the guidance or direction to make and use the full scope of claimed invention without undue experimentation for one skilled in the art. For the reasons above and the previous office action, the instant rejection is maintained.

Conclusion

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander D. Kim whose telephone number is (571) 272-5266. The examiner can normally be reached on 11AM-7:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alexander D Kim/
Examiner, Art Unit 1656

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652

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